Homogeneous photochemical oxidation *via* singlet O_2 in supercritical CO_2

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This communication describes the reaction chemistry of singlet oxygen in supercritical carbon dioxide, demonstrating rapid and quantitative conversion of α-terpinene to ascaridole.

Singlet oxygen ($^1O_2$) is highly reactive towards organic compounds and has found applications in a wide range of synthetic reactions.[1] $^1O_2$ is short-lived and can be generated by either chemical or photochemical processes. One approach uses the photosensitisation of the triplet ground state; common photosensitisers include organic dyes such as methylene blue[2] and rose bengal, porphyrins and phthalocyanines, semi-conductors,[3] and transition metal complexes.[1b] The Twelve Principles of Green Chemistry[4] are particularly relevant when considering photochemistry as a method for reduced usage of reagents, lower reaction temperatures and improved selectivity. Dye-sensitised photo-oxygenation only requires low energy irradiation and involves complete incorporation of O_2 into the product.

Supercritical carbon dioxide ($scCO_2$) offers a number of advantages as a medium for performing oxidation chemistry with molecular O_2. It is fully oxidised and hence non-flammable and non-toxic. Supercritical fluids are completely miscible with gaseous O_2 and have lower viscosity and higher diffusivity than more conventional solvents. These properties can enable reactions to proceed without the mass transport limitations often found in traditional multi-phase systems.[5] Oxidation reactions in $scCO_2$ using molecular O_2 and metal catalysts[6] have been successfully performed and highlight the advantages described above.

Photophysical investigations[7] have demonstrated that it is possible to generate $^1O_2$ in $scCO_2$. $^1O_2$ was shown to have a long lifetime in $scCO_2$ (5.1 ms at 14.7 MPa and 314 K) and this lifetime was found to be dependant upon the density of the $scCO_2$. Of course $scCO_2$ has other potential advantages as a medium for reaction chemistry, *e.g.* ease of recovery of products.[8]

Many of the sensitisers commonly used for organic synthesis are virtually insoluble in $scCO_2$, *e.g. meso*-tetraphenylporphyrin (TPP). Fluorination often greatly increases the solubility[9] of such compounds in $scCO_2$ and Co- and Zn-based fluorinated porphyrins have been shown to have high solubility in $scCO_2$.[10] In this communication we report the use of a perfluorinated analogue of TPP, 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin, TPFPP (see Fig. 1), as an efficient photosensitiser for carrying out photo-oxidation in $scCO_2$.

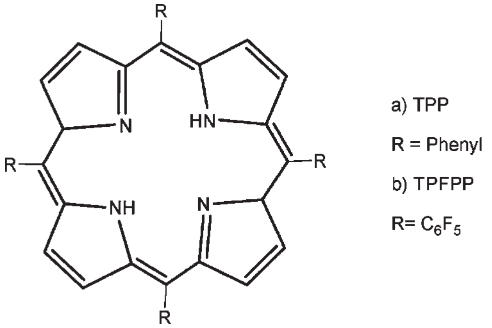

Fig. 1 Structure of (a) *meso*-tetraphenylporphyrin (TPP) and (b) 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (TPFPP). TPFPP was chosen due to its highly fluorinated nature which is known to impart solubility in $scCO_2$.

We have studied the reaction of α-terpinene with $^1O_2$ to form ascaridole. The experimental apparatus used for these experiments is shown schematically in Fig. 2.

All reactions were performed using a multi-purpose photochemical and spectroscopic cell,[11] with CaF_2 windows and a path-length of *ca.* 2 mm. Experiments were carried out by dilution of the O_2 with $scCO_2$ prior to pressurising the photochemical cell. This dilution lowers the concentration of O_2 and reduces the chance of the explosion limits of the reaction system being exceeded.‡ TPFPP (4.1 μmol) was dissolved overnight in α-terpinene (6.1 mmol) and 30 μL of this solution was injected into the empty cell. The cell was then charged with a mixture of $scCO_2 + O_2$ of known molar composition as shown in Fig. 2. This design of the gas-mixing is based on the apparatus used previously for hydrogenation in $scCO_2$.[8]

We have tested our approach with the reaction of α-terpinene with $^1O_2$ to form ascaridole, a process easily monitored using FTIR, Fig. 3a. At 140 bar with 1.31 mol% O_2 in $scCO_2$, quantitative conversion of α-terpinene was observed within 160 s. Conversion was confirmed independently by ^1H NMR spectroscopy. The reaction proceeds rapidly with a pressure drop caused by the consumption of O_2 at a rate consistent with the zero order kinetics deduced from the FTIR measurements, Fig. 3b. The zero order kinetics are consistent with the rate of

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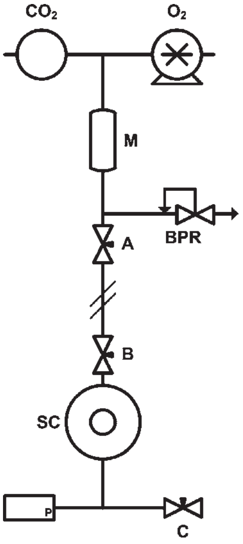

Fig. 2 Schematic of the reactor system. $\mathbf{CO_2}$ is delivered from a chilled Jasco™ PU-1580-CO_2 pump and O_2 is added at a measured rate *via* a Rheodyne dosage unit. The CO_2 + O_2 are passed through the mixer, **M**, (two 5 cm 1/4 inch SS316 tubes at 50 °C) and are then flowed out continuously *via* a **Jasco**™ BP-1580-81 back pressure regulator, **BPR**. The reaction cell, **SC**, is loaded with substrate + photosensitiser and is then filled with CO_2 + O_2 by opening valves **A** and **B** and allowing the system to reach the pressure maintained by the **BPR**. Finally, the cell is isolated by closing taps **A** and **B**; the pressure inside the sealed cell is monitored *via* the transducer, **P**.

absorption of light being the key factor in determining the overall rate of reaction.

This rapid and quantitative conversion in $scCO_2$ is encouraging because it offers potential of scale-up using either batch or continuous systems. We have made preliminary measurements comparing the rates of reaction in $scCO_2$ and CCl_4 using either TPP or TPFPP with the same cell/light source for both solvents. The rate with TPFPP is *ca.* ×2 slower than in $scCO_2$, Table 1, entries 1–3.

In $scCO_2$, the reaction is run with a modest excess of O_2, entry 3. We found that increasing the amount of O_2 had negligible effect on the TOF (entries 4–6) suggesting that mass transport of O_2 may not be a limiting factor in this reaction, an observation consistent with the zero order kinetics found above.

We have also investigated the effect of pressure upon the reaction rate in $scCO_2$ by charging the cell with 1.31 mol% O_2 and $scCO_2$ mixture at 80 bar. More CO_2 was then added to this baseline system to increase the pressure whilst keeping a constant amount of O_2. The solubility of TPFPP was probed using UV/Vis spectroscopy monitoring the Soret band at 390 nm, while the overall phase behaviour was monitored in a separate variable volume view cell. The results of these measurements are combined in Fig. 4.

Our batch reactor in which the TOF was measured differs from the view cell in two ways; it has no stirrer and the windows have a smaller diameter than that of the cell. This means that, if the pressure is low and the mixture biphasic, the liquid phase will be at the bottom of the cell and out of direct sight of the photolysis lamp. Thus, at 80 bar, there was little conversion of α-terpinene to ascaridole, Fig. 4(a), which is understandable from Fig. 4(b) which shows that TPFPP and α-terpinene are largely insoluble in the gas phase at this pressure. The TOF increases as the pressure is increased to 120 bar but then remains relatively constant up to 200 bar. This increase in TOF correlates with the solubility of TPFPP in $scCO_2$ until full dissolution of the photosensitiser in the supercritical solvent. Thus, the TOF is lower at low pressure because much of the TPFPP will be in the liquid phase and hence, within a given time interval, fewer photons will be

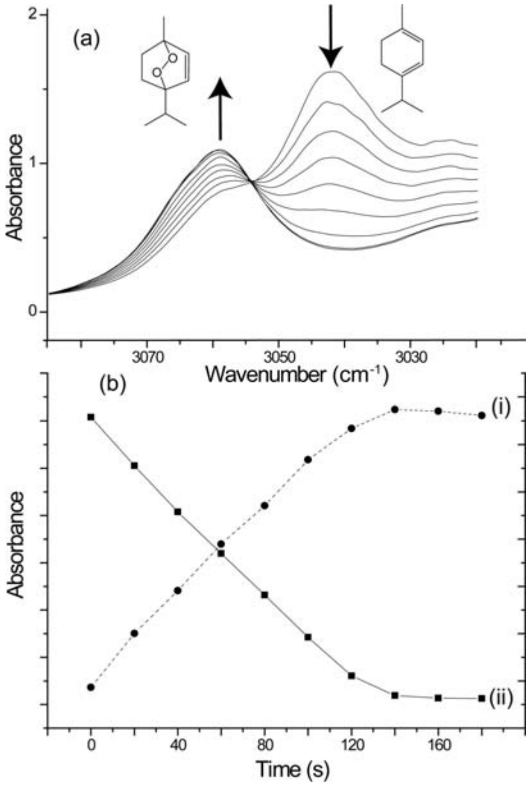

Fig. 3 (a) FTIR monitoring the reaction of α-terpinene (0.184 mmol) with O_2 (140 bar, 1.31 mol%) in $scCO_2$ (140 bar) at 40 °C during irradiation (300 W xenon lamp with a filter to cut out UV irradiation). Spectra were recorded at 20 s intervals showing formation of ascaridole (3060 cm^{-1}) and loss of starting material (3042 cm^{-1}); (b) kinetic traces obtained by plotting the band maxima at (i) 3060 cm^{-1} and (ii) 3042 cm^{-1} *versus* irradiation time

Table 1 Turnover frequencies for the photo-oxidation of α-terpinene in CCl_4 and in $scCO_2$ at 40 °C

	Photosensitiser	Solvent system	O_2 : substrate ratio	Substrate : photosensitiser (mol : mol)	TOF/ s^{-1}
1	TPP	CCl_4	2.1 bar[a]	1500	3
2	TPFPP	CCl_4	2.6 bar[a]	1500	7
3	TPFPP	140 bar CO_2	1.1	1500	16
4	TPFPP	140 bar CO_2	1.1	750	12
5	TPFPP	140 bar CO_2	2.1	750	11
6	TPFPP	140 bar CO_2	3.3	750	11

[a] CCl_4 presaturated with O_2 and atmosphere of pure O_2 above at the shown pressure resulting in a biphasic mixture. Full conversion observed and initial rate used to calculate TOF as kinetics deviated from zero order after *ca.* 90 s.

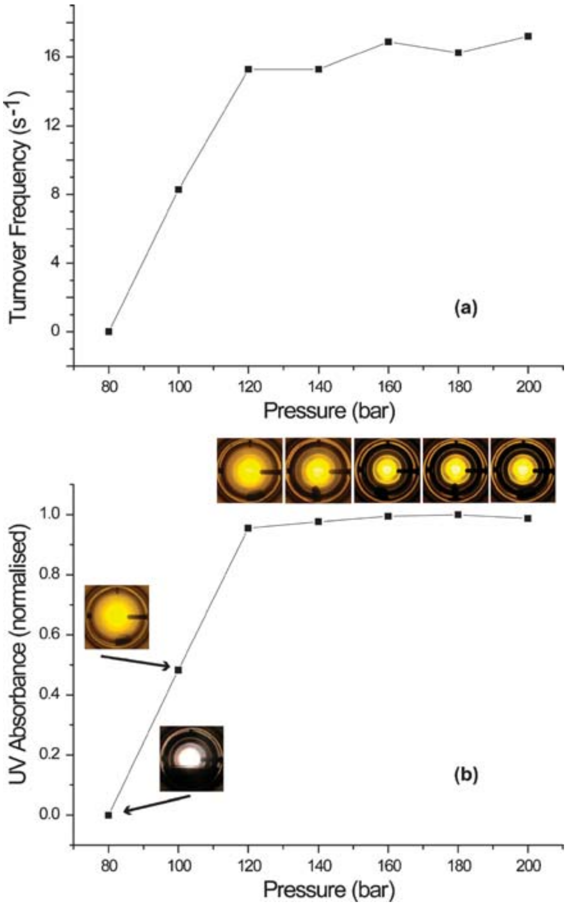

Fig. 4 (a) Plot of turnover frequency (TOF) for the reaction of α-terpinene with $^1O_2$ *vs.* pressure of $scCO_2$ at a constant concentration of O_2. (b) Plot of the concentration of dissolved TPFPP *vs.* pressure, as monitored by the UV/Vis absorbance at 390 nm. The photographs show the phase behaviour at the different pressures in a variable volume view cell.

absorbed than under monophasic conditions at higher pressure when the TPFPP and the substrate are fully dispersed throughout the volume of the batch reactor.

We have performed preliminary reactions in a continuous flow system using a tubular sapphire reactor. We achieved 89% conversion to product at a flow rate of 0.1 ml min^{-1} of reactant even without full optimisation (*i.e. ca.* 1 mL of product in 10 min). The use of surfactants has indicated that one can also carry out reactions with non-fluorinated sensitisers such as the traditional methylene blue. Both of these approaches will be the subject of a future publication.

In this communication, we have reported an organic transformation of $^1O_2$ in $scCO_2$ with a perfluorinated porphyrin as a photosensitiser which is soluble in high pressures of $scCO_2$. Quantitative photochemical oxygenation of α-terpinene was achieved in less than 3 min. Preliminary results indicate that other reactions of $^1O_2$ can be carried out in $scCO_2$ including the oxidation of 2,3-dimethylbut-2-ene to 3-hydroperoxy-2,3-dimethylbut-1-ene. Thus, $scCO_2$ provides a non-chlorinated and totally non-flammable solvent for performing photochemical $^1O_2$ reactions. We are now exploring the use of less expensive sensitisers, establishing which other reactions of $^1O_2$ can benefit from the use of $scCO_2$ and investigating possible ways of scaling these reactions up.

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Notes and references

‡ **Safety warning**: these reactions involve high pressures and should only be carried out in an apparatus with the appropriate pressure rating and with due regard to the potentially explosive reaction between oxygen and organic compounds.

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